Remarks

Reconsideration of this Application is respectfully requested.

Claims 1-13, 17, 19-32, and 45-70 are pending in the present application, with claims 1 and 45 being the independent claims. Claims 1 and 45 have been amended to clarify the nature of the claimed invention and to incorporate the limitations of claims 12 and 53, respectively. Claims 5, 6, 49, and 50 have been amended to clarify which steps within the independent claims to which they refer. Support for the claims can be found throughout the specification, *inter alia*, in the claims as originally filed. Claims 12 and 53 have been canceled without prejudice to or disclaimer of the subject matter presented therein. These amendments are sought to place the claims into condition for allowance or for consideration on appeal, and introduce no new matter. Entry and consideration of these amendments are respectfully requested.

Based on the following remarks, Applicants respectfully request that the Examiner reconsider the outstanding rejection and that it be withdrawn.

Rejection Under 35 U.S.C. § 103(a)

The rejection of claims 1-13, 17, 19-32 and 45-70 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Dang *et al.*, (U.S. 2003/0119107 A1; hereinafter "Dang") in view of Yan *et al.*, (U.S. 2003/0027331; hereinafter "Yan") and Kehat *et al.*, (The Journal of Clinical Investigation, Vol. 108, No. 3, p. 407-414; hereinafter "Kehat") has been maintained. Applicants traverse the rejection, especially as it may be applied to the amended claims presented herein.

The Examiner maintains the rejection, in part, because there is no limitation in the claims that the ES cells cannot be encapsulated (Office Action, p. 4). Therefore, "the stirred encapsulated ES cell suspension culture as taught by Dang can also be considered as a type of liquid single cell suspension culture." (*Id.*) Not in acquiescence to the propriety of the rejection, but rather solely to advance prosecution, Applicants have amended claims 1 and 45 to clarify that no encapsulation step occurs during the claimed methods.

The Examiner further asserts that the claims do not recite superior results to the conventional methods. Not in acquiescence to the propriety of the rejection, but rather solely to advance prosecution, Applicants have amended claims 1 and 45 to clarify the resulting amounts of EBs formed by the claimed method.

With respect to the Examiner's statement "[*I*]*n fact, Dang teaches stirred ES cell culture (e.g. [0162], [0163]). Encapsulation of ES cells is used to prevent cell aggregation and to obtain higher number of EBs at higher cell density. Thus, in view of the teachings of Dang and the state of prior art, it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to rock a liquid single cell suspension of pluripotent cells and there is reasonable expectation to obtain embryoid bodies and differentiation of ES cells to cardiomyocytes as claimed.*" (Office Action, p. 4), Applicants respectfully disagree. Applicants respectfully point out that in the experiments referred to by the Examiner (paragraphs [0162] and [0163] of Dang), the concentration of ES cells per ml is at least one magnitude lower than required in the method of the presently claimed invention (Dang, p. 16 in tables 4 (reproduced below) and 5 referred to in paragraph [0162] and [1016]).

TABLE 4

EB Efficiency in liquid culture (LSC), stirred culture (SC), and encapsulated stirred culture (ESC). Cultures were initiated with 10^3 or 10^4CCE ES cells/ml and analyzed after 7 days of differentiation. EB efficiency in LSC declined as cell density increased. Aggregation occurred readily in SC regardless of cell concentration. Encapsulation effectively controlled cell aggregation, maintaining a high EB efficiency in stirred culture.

	LSC	SC	ESC
10^3 ES cell/ml	42 ± 9%	>0.1%	41 ± 21%
10^4 ES cells/ml	8.5 ± 2.7%	>0.1%	35 ± 3%

Furthermore, Applicants respectfully assert that closer inspection of the results shown in Table 4 of Dang, reveals that, though less pronounced, ***EB efficiency drops at higher cell density*** even in the encapsulated stirred culture (ESC). Accordingly, the skilled artisan would not have envisaged that EB efficiency, using a higher cell density, for example 10^5 cells/ml instead of 10^4 as shown in Table 4, would improve by omitting the encapsulation step and rocking the culture according to the claimed method, as opposed to the method described in Dang. Thus, Applicants respectfully assert that it is untenable to combine the method of Dang, which necessarily includes encapsulation of the ES cells and teaches low cell density, with Yan and Kehat, which disclose different methods of ES cell culturing at higher density, but certainly do not employ encapsulation. Accordingly, for at least the reasons stated above, Applicants respectfully request that the rejection be reconsidered and withdrawn.

Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Reply is respectfully requested.

Respectfully submitted,

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